Remarks

Prior to the amendments herein, claims 1-10, 12-21, 23, 25-27, 29-37 and 39-52 were pending in this application. Claims 39-52 are withdrawn from consideration. Claims 4, 15 and 35 are canceled herein without prejudice. A Request for Continued Examination under 37 C.F.R. § 114 is submitted herewith, along with a Supplemental Information Disclosure Statement, in accordance with 37 C.F.R . § 1.56, disclosing a reference that has recently come to the attention of applicants. Applicants acknowledge withdrawal of numerous previous objections and rejections. Applicants also express their appreciation for the Examiner's participation in a telephonic interview with the undersigned on April 1, 2004.

Further, claims 1-3, 9-10, 12-14, 20-21, 23, 25-27, 29-34 and 36-37 are amended herein for clarity. Support for these amendments can be found in the original claim language and throughout the specification, as set forth below. It is believed that these amendments add no new matter. In light of these amendments and the following remarks, applicants respectfully request entry of these amendments.

Formal Matters

The specification is objected to for the recitation of "$H^{7(1)}$, $G^{10(4)}$..." as allegedly being unclear what is meant. The specification is amended herein by deleting the superscripts and by substituting therefor text that explains the meaning of these superscripts as set forth on page 17, lines 25-29. No new matter is believed to be added. Therefore, applicants respectfully request withdrawal of this objection.

35 U.S.C. § 112, first paragraph

Claim 31 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner states that claim 31 recites the limitation "exclude hepatocyte growth factor," but the Examiner was unable to find support in the specification where applicants had pointed out the support.

Claim 31 is amended herein by deleting the phrase "exclude hepatocyte growth factor." Applicants believe that this rejection is overcome and respectfully request withdrawal of this rejection.

35 U.S.C. § 112, second paragraph

A. Claims 1-10, 12-21, 23, 25-27 and 29-37 remain rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention, based on the term "substantially homologous."

With regard to GLP-1, claims 1, 23, 31, 32 and 34 are amended herein by deleting the phrase "growth factors having amino acid sequences substantially homologous to GLP-1" and substituting therefor the phrase "a GLP-1 peptide, a GLP-1 peptide containing one or more conservative amino acid substitutions at positions other than positions 7, 10, 12, 13 and 15 of GLP-1, and a fragment of the preceding GLP-1 peptides." With regard to exendin-4, claims 12, 27, 31, 33 and 36 are amended herein by deleting the phrase "growth factors having amino acid

sequences substantially homologous to exendin-4" and substituting therefor the phrase "an Exendin-4 peptide, an Exendin-4 peptide containing one or more conservative amino acid substitutions at positions other than positions 1, 4, 6, 7 and 9 of Exendin-4, and a fragment of the preceding Exendin-4 peptides." Support can be found in the specification on page 15, line 30 to page 16, line 14. Applicants believe that these amendments overcome the rejections and respectfully request withdrawal of these rejections.

B. Claim 31 is further rejected because the Office Action alleges that it is unclear what "$H^{7(1)}$, $G^{10(4)}$..." means. Applicants believe it is clear what the superscripts mean because a person of skill would read the specification and understand what is meant. Nevertheless, in order to expedite prosecution of the pending application, claim 31 is amended herein by deleting the superscripts and substituting therefor text that explains the meaning of the superscripts. Moreover, the specification is amended herein so that the claim language of amended claim 31 conforms to the language in the amended specification. Support can be found in the specification on page 17, lines 25-29.

35 U.S.C. § 112, first paragraph

A. Claims 1-10, 12-21, 23, 25-27 and 29-37 remain rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for claims limited in scope to an isolated population of insulin-producing cells made by contacting GLP-1 or exendin-4, allegedly does not reasonably provide enablement for claims to an isolated population of insulin-producing cells made by contacting growth factors having amino acid sequences *substantially homologous* to GLP-1 or exendin-4, or *fragment* thereof.

Claims 1, 12, 23, 27, 31-34 and 36 are amended herein by deleting the phrase "growth factors having amino acid sequences substantially homologous to" and substituting therefor the phrase "a GLP-1 peptide, a GLP-1 peptide containing one or more conservative amino acid substitutions at positions other than positions 7, 10, 12, 13 and 15 of GLP-1, and a fragment of the preceding GLP-1 peptides" in claims 1, 23, 32 and 34. In claims 12, 27, 33 and 36, the phrase "an Exendin-4 peptide, an Exendin-4 peptide containing one or more conservative amino acid substitutions at positions other than positions 1, 4, 6, 7 and 9 of Exendin-4, and a fragment of the preceding Exendin-4 peptides" is substituted for the deleted phrase. In claim 31, the deleted phrase is substituted by both phrases, "a GLP-1 peptide, a GLP-1 peptide containing one or more conservative amino acid substitutions at positions other than positions 7, 10, 12, 13 and 15 of GLP-1, and a fragment of the preceding GLP-1 peptides" and "an Exendin-4 peptide, an Exendin-4 peptide containing one or more conservative amino acid substitutions at positions other than positions 1, 4, 6, 7 and 9 of Exendin-4, and a fragment of the preceding Exendin-4 peptides." Support can be found in the specification on page 15, line 30 to page 16, line 14.

The specification discloses the structures of GLP-1 and several fragments thereof, each of which has an H residue at position 7, a G residue at position 10, an F residue at position 12, a T residue at position 13 and a D residue at position 15. The specification further discloses the structures of exendin-4 and several fragments thereof, each of which has an H residue at position 1, a G residue at position 4, an F residue at position 6, a T residue at position 7 and a D residue at position 9. See in the specification page 16, line 24 to page 18, line 2.

Thus, a person of skill, after reading the specification at the time the application was filed, would be able to practice the invention by selecting a substance selected from the group

consisting of a GLP-1 peptide, a GLP-1 peptide containing one or more conservative amino acid substitutions at positions other than positions 7, 10, 12, 13 and 15 of GLP-1, and a fragment of the preceding GLP-1 peptides. Moreover, a person of skill would be able to practice the invention by selecting a substance selected from the group consisting of an Exendin-4 peptide, an Exendin-4 peptide containing one or more conservative amino acid substitutions at positions other than positions 1, 4, 6, 7 and 9 of Exendin-4, and a fragment of the preceding Exendin-4 peptides.

Applicants believe that the scope of amended claims 1, 12, 23, 27, 31-34 and 36 and dependent claims 2-10, 13-21, 25-26, 29-30, 35 and 37 is commensurate with the teachings of the specification and that these rejections are overcome. Therefore, applicants respectfully request withdrawal of these rejections.

B. Claims 1, 12, 23, 27, 31-34, and 36 remain further rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

As described above, claims 1, 12, 23, 27, 31-34 and 36 are amended herein by deleting the phrase "growth factors having amino acid sequences substantially homologous to ... " and substituting therefor the phrase "a GLP-1 peptide, a GLP-1 peptide containing one or more conservative amino acid substitutions at positions other than positions 7, 10, 12, 13 and 15 of GLP-1, and a fragment of the preceding GLP-1 peptides" and/or the phrase "an Exendin-4 peptide, an Exendin-4 peptide containing one or more conservative amino acid substitutions at

positions other than positions 1, 4, 6, 7 and 9 of Exendin-4, and a fragment of the preceding Exendin-4 peptides." Further, the claims are amended by reciting five essential amino acid residues that are present and conserved in a GLP-1 peptide and fragments thereof, and an exendin-4 peptide and fragments thereof.

The Written Description Guidelines, effective as of January 5, 2001, state "[w]hether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." See 3(c)(ii).

Applicants provide detailed, known referent structures, *i.e.*, the amino acid sequences of GLP-1, exendin-4, and fragments thereof, all of which comprise five essential amino acid residues at specified positions in the amino acid sequences and have the differentiating function. Moreover, a person of skill would know how to visualize and make the claimed substances that can have conservative substitutions of the amino acid residues, except for the five essential amino acid residues located at their respective positions. Thus, substantial structure is indeed provided. Applicants also teach that the common function of these substances is the differentiation of non-insulin-producing cells into insulin-producing cells. Further, applicants teach how to make the claimed substances. See in the specification, page 15, line 30 to page 16, line 14. Thus, because structure and common function are described in the specification, one of

skill in the art would recognize that applicants were in possession of the claimed substances at the time of the filing of the application. Applicants, therefore, respectfully request reconsideration and withdrawal of this rejection.

35 U.S.C. § 102

Claims 23, 26, 27, 30, 31 and 35-37 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Eng (U.S. Patent No. 5,424,286) for the reasons set forth in the previous Office Actions, paper Nos. 10 and 15.

Claim 35 is canceled herein, thereby rendering moot this rejection as it applies to this claim.

The art cited by the Examiner does not teach contacting a population of non-insulin-producing cells with a substance for at least twenty-four hours. Moreover, claims 23, 27, 31 and 36 are amended herein to recite the phrase "an amount of a substance effective to induce insulin production." Thus, even if a trace amount of a substance that can induce insulin production were present in the subjects disclosed in the prior art, the art fails to teach contacting the cells with an effective amount of a substance such that insulin production is induced. As the cited art fails to teach every limitation of the claim, applicants believe the rejections are overcome and respectfully request their withdrawal.

Pursuant to the above amendments and remarks, reconsideration of the pending claims is believed to be warranted, and such action is respectfully requested. The Examiner is invited to directly contact the undersigned if such contact may enhance the efficient prosecution of this application.

Credit Card Payment Form PTO-2038 authorizing payment in the amount of $1,900.00 (representing a $950.00 three-month extension of time fee to extend the period for response by three months, i.e., to July 13, 2004; a $770.00 Request for Continued Examination (RCE) fee under 37 C.F.R. § 1.17(e)); and a $180.00 fee under 37 C.F.R. § 1.17(p)) is enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required or to credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Tina W. McKeon

July 13, 2004
Date